Ultrasonography for Assessment of Subcutaneous Nodules

SELIM NALBANT, HECTOR COROMINAS, BENJAMIN HSU, LAN X. CHEN, H. RALPH SCHUMACHER, and TASANEE KITUMNUAYPONG

ABSTRACT. ***Objective.*** To characterize a variety of subcutaneous lesions by their ultrasonographic (US) appearance, and establish these images as a starting point to measure changes with treatments.

Methods. Twenty-six patients with 48 subcutaneous nodular swellings of various types were imaged using a portable US machine equipped with a 10 MHz linear transducer. All patients had a known diagnosis of a rheumatic disease. We used US to examine subcutaneous lesions and the underlying cortical surface of the bone or joint. Two measurements of some tophi and rheumatoid nodules were done on different dates to examine reproducibility of the measurements.

Results. Nodular lesions included 20 tophi and 20 rheumatoid nodules, 2 sarcoid nodules, 2 lipomas, and 4 synovial cysts. Tophi most often appeared as heterogeneous masses; hypoechoic areas in 2 tophi were decreased after aspiration of chalky liquid tophaceous material. Occasionally tophi had calcifications appearing hyperechoic with acoustic shadowing. Cortical bone erosions could be seen adjacent to some tophi. The nodules in patients with rheumatoid arthritis were often attached closely to the bone surface and less erosive to bone, allowing the cortical bone to be seen easily. The nodules were more homogeneous. Some showed a central sharply demarcated hypoechoic area, possibly corresponding to necrosis inside the rheumatoid nodules. Nodules were easily measured. The repeated measurements of both tophi and rheumatoid nodules showed excellent reproducibility. Lipomas had different echogenic patterns depending on composition of the associated connective tissue and position of the mass. They could be hypoechogenic, hyperechogenic, or mixed, but were easily distinguished by oval shapes with well demarcated capsules. Synovial cysts seen in this study had a characteristic hypoechoic pattern.

Conclusion. Subcutaneous nodules examined by sonography show characteristics and patterns that, although not diagnostic, can be used to help distinguish their etiology. Tophi and rheumatoid nodules can be easily measured and these measurements used to help follow disease progression or response to therapy. (J Rheumatol 2003;30:1191–5)

Key Indexing Terms:
ULTRASONOGRAPHY SUBCUTANEOUS NODULES TOPHI
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Subcutaneous nodules are commonly seen in rheumatologic patients. Some can be distinguished by combining history and examination, some need further investigation by magnetic resonance imaging (MRI) or computed tomography (CT), biopsy, or aspiration[1,2].

The recent technological advances in musculoskeletal sonography with faster computers and higher frequency transducers allow one to clearly depict soft tissue masses[3,4] as well as to detect pathological changes of synovium, cartilage, and the bone surface[5-7]. This can be done easily in the clinic; ultrasonography (US) is not invasive and causes no radiation exposure[8-11]. Sonography can be an important clinical tool to confirm and decide proper management for the patient.

US is good for detecting soft tissue swelling and can effectively differentiate cystic from solid masses[3,12]. Some studies have reported the advantage of US in identification of rheumatoid nodules[13,14], epidermal cysts[15], or xanthomas[16]. One small study examined possible distinguishing features of tophi and rheumatoid nodules[17]. Why do we not use this for evaluation of any soft tissue mass in our rheumatologic patients[13]? Sonography can provide clues for diagnosis, and can be used for followup, although US use in this clinical field is still in its infancy in the USA.

We describe the characteristics of some soft tissue nodules, such as tophi, rheumatoid nodules, lipomas, and synovial cysts, that are commonly seen in our clinics.

From the Rheumatology Division of the Hospital of the University of Pennsylvania and the Rheumatology Section of the Philadelphia Veterans Affairs Medical Center, Philadelphia, Pennsylvania, USA.

S. Nalbant, MD, Rheumatology Research Fellow; H. Corominas, MD, Rheumatology Fellow; B. Hsu, MD, Rheumatology Fellow; L.X. Chen, MD, PhD, Rheumatology Fellow, University of Pennsylvania; H.R. Schumacher Jr, MD, Professor of Medicine, University of Pennsylvania, Chief of Rheumatology, Philadelphia VA Medical Center; T. Kitumnuaypong, MD, Rheumatology Research Fellow, University of Pennsylvania.

Address reprint requests to Dr. H.R. Schumacher Jr, VA Medical Center, University and Woodland Avenue, Philadelphia, PA 19104-4283. E-mail: schumacr@mail.med.upenn.edu

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MATERIALS AND METHODS

Patients. We enrolled 26 patients with rheumatic disease and 48 nodules or suspected nodules from regular attendees at the rheumatology clinic at the Hospital of the University of Pennsylvania or Philadelphia VA Medical Center during May to October 2001. Fifteen patients (numbers 1–15) had known rheumatoid arthritis (RA) and fulfilled the American College of Rheumatology revised criteria for RA[18], 10 had gout (patient numbers 16–25) confirmed by identification of monosodium urate (MSU) crystals in the tophi or from a joint fluid, and one patient (number 26) had sarcoidosis, diagnosed both histologically and clinically. In RA and gout, the nodules were found mostly overlying joint areas such as the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and metatarsophalangeal (MTP) joints and other pressure areas such as the elbow. There were 2 nodules on the back and anterior chest wall, 4 soft palpable masses in the popliteal area of patients with RA, and 2 nodules on the preauricular area.

Ultrasound study. All patients underwent sonography for characterization of the subcutaneous nodules by 2 rheumatologists trained in musculoskeletal US and with experience using portable US. The equipment used was a SonoSite™ 180 (SonoSite, Bothell, WA, USA) hand-carried ultrasound, 10-5 MHz and 38 mm, broadband linear array transducer. Sonograms of subcutaneous nodules were obtained in transverse and longitudinal planes. The lengths and widths of the lesions were measured using electronic calipers. We had 2 measurements for both width and length. Final measurements presented are means of these measurements. Repeated area measurements were also done within 2 days for 3 patients each from the tophus and RA nodule groups to examine the reproducibility of the results. We also described shape, echogenicity, posterior acoustic shadowing, and presence or absence of underlying cortical bone surface involvement. The nodules had been characterized into groups according to clinical diagnosis.

Statistical analysis. All data are expressed as mean ± SD. Paired results were analyzed using the marginal homogeneity test or Wilcoxon ranks test for matched pairs. P values less than 0.05 were considered significant.

RESULTS

The tophi in gout were commonly found at the elbow and more than one location was often involved (Table 1). Most were irregularly shaped, especially when there was associated bursitis (Figure 1). All patients with associated bursitis had gout. The gouty nodules appeared as heterogeneous (80%) masses, composed of hypoechoic and hyperechoic areas with generally more of the tophus being hyperechoic. Occasional tophi showed a posterior acoustic shadow (Table 2). The posterior acoustic shadowing was significantly more frequent for gout than RA ($p = 0.025$). After 2 of the tophi were aspirated and liquid chalky material obtained, the size of the hypoechoic areas was decreased. Cortical bone erosions (Figure 2A) were seen adjacent to some gouty tophi and these were more frequent than with RA nodules ($p = 0.003$).

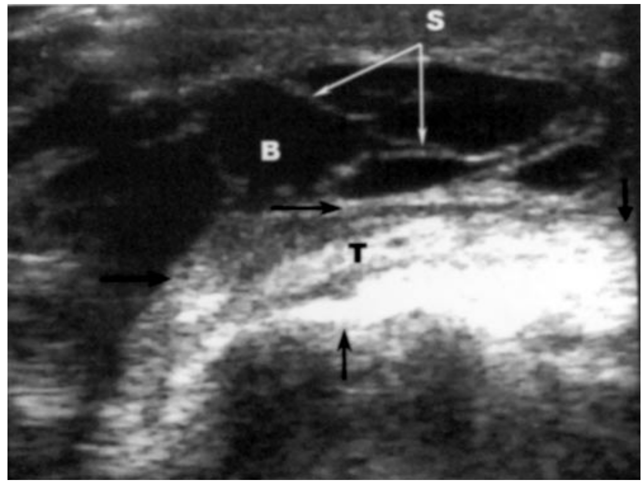


Figure 1. Elbow tophus with overlying bursitis, longitudinal view. The tophus (T) has a heterogeneous appearance with hypoechoic and hyperechoic areas. Black arrows denote the margins of the tophus. Bursitis (B) is homogeneous and hypoechoic, except for hyperechoic linear septae (S) (patient 16).

We studied 20 RA nodules in 13 patients. The nodules appeared as oval, generally homogenous (85%), hypoechoic (85%) masses that were attached closely to the bone surface and less erosive to bone (Table 2, Figure 3) than gouty tophi. Four patients showed a centrally sharply demarcated, very hypoechoic area.

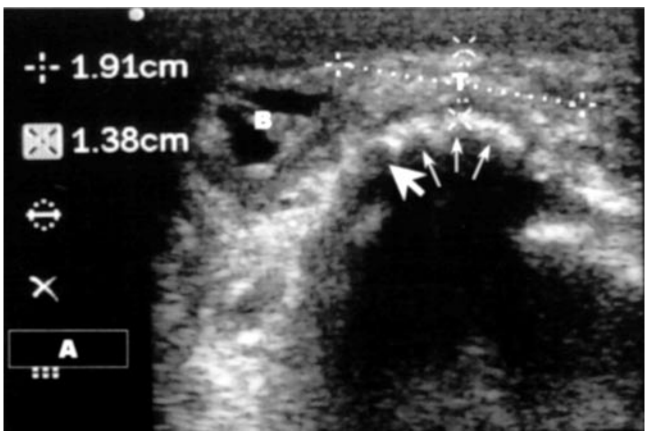
Table 1. Demographic and clinical features of the patients with tophi and rheumatoid nodules.We studied more than 1 nodule per patient.

Variable	RA (Patients 1–13) n = 13	Gout (Patients 16–25) n = 10	p
Age, yrs, mean ± SD	56.54 ± 7.01	61.3 ± 8.45	0.71
Disease duration, yrs, mean ± SD	9.23 ± 3.14	10.7 ± 3.13	0.11
Number and location of nodules			
PIP, MCP, DIP	9	4	0.13
MTP	3	6	0.3
Elbow	6	10	0.12
Wrist	2	0	—
Size of nodules, (cm) (width x length), mean			
PIP, MCP, DIP	1.1 x 0.5	0.8 x 0.5	0.23
MTP	2.9 x 1.8	1.6 x 1.2	0.26
Elbow	2.7 x 1.6	2.9 x 2.1	0.09
Wrist	2.1 x 1.3	0	—

DIP: distal interphalangeal joints; PIP: proximal interphalangeal joints; MCP: metacarpophalangeal joints; MTP: metatarsophalangeal joints.

Table 2. Ultrasonographic evaluation of rheumatoid nodules and tophi.

Image	Rheumatoid Nodules (Patients 1–13) (RA = 20)	Tophi (Patients 16–25) (Gout = 20)	p
Density			
Homogeneous (%)	17 (85)	4 (20)	0.007
Heterogeneous (%)	3 (15)	16 (80)	< 0.001
Echogenicity			
Hypoechoic (%)	17 (85)	5 (25)	0.003
Hyperechoic (%)	3 (15)	15 (75)	0.001
Post acoustic shadow	1	5	0.025
Adjacent tissues			
Cortical bone irregularity	5	9	0.003
Bursitis	0	3	—



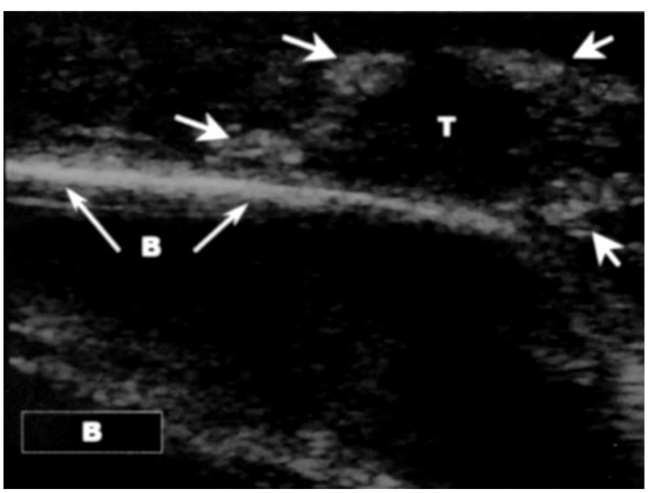


Figure 2. (A) Elbow tophus (patient 18), transverse view. The tophus (T) is very close to the bone, but bone and tophus are separate from each other. There is a cortical bone irregularity (arrows), which is most definite near the bursa (B). This bursa has a characteristic homogeneous hypoechoic appearance surrounded by a hyperechoic thicker wall. (B) Elbow tophus (patient 19), longitudinal view. This tophus (T) is very close the bone (B), but there is no bone irregularity. Arrows mark margins of the tophus. These 2 pictures illustrate bone irregularity and integrity on US appearance.

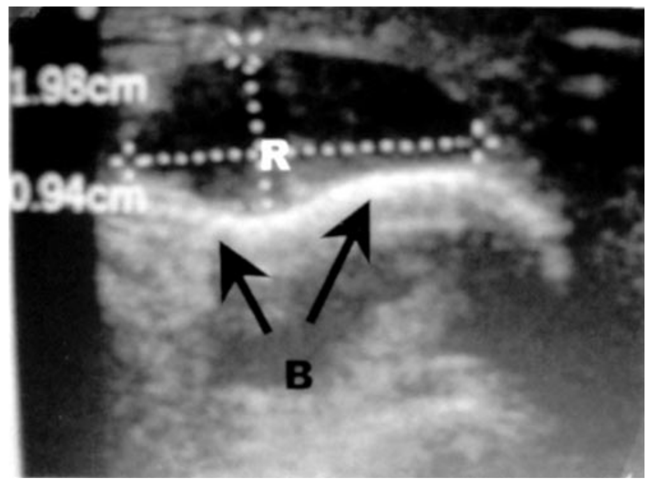


Figure 3. Elbow rheumatoid nodule, transverse view. The nodule (R) has an oval, hypoechoic, homogeneous appearance. It is very close to the bone (B), but no destruction or irregularity is seen (patient 1).

The transverse (first 0.49 ± 0.25 cm^2 and second 0.44 ± 0.23 cm^2) and longitudinal (first 2.28 ± 3.46 cm^2 and second 2.42 ± 3.71 cm^2) repeated measurements of 3 patients each from the tophus and RA nodule groups showed there was no significant difference between 2 measurements (p = 0.27 and 0.17).

Two patients with RA (numbers 14 and 15) had rheumatoid nodular masses at unexpected sites, namely the anterior chest wall and back. The sizes were 2.5 and 1.5 cm and these were clinically felt to be most compatible with lipomas. The sonographic image of one was hypoechogenic and the other was hyperechogenic. Both had oval shape and well demarcated capsules (Figure 4).

Two nodular masses were at the preauricular area of the patient with sarcoidosis. The sizes were 1.5 and 1 cm, respectively. Nodules had an irregular, oval, and hypoechoic US appearance. They were close to bone but no bone erosion was seen (Figure 5).

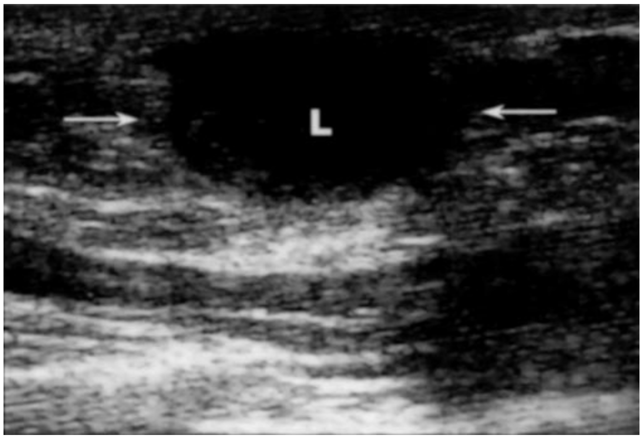


Figure 4. Lipoma on chest wall (patient 14). The lipoma (L) has a hypoechoic, well demarcated, homogeneous appearance. The margin is not as hyperechoic as in a rheumatoid nodule.

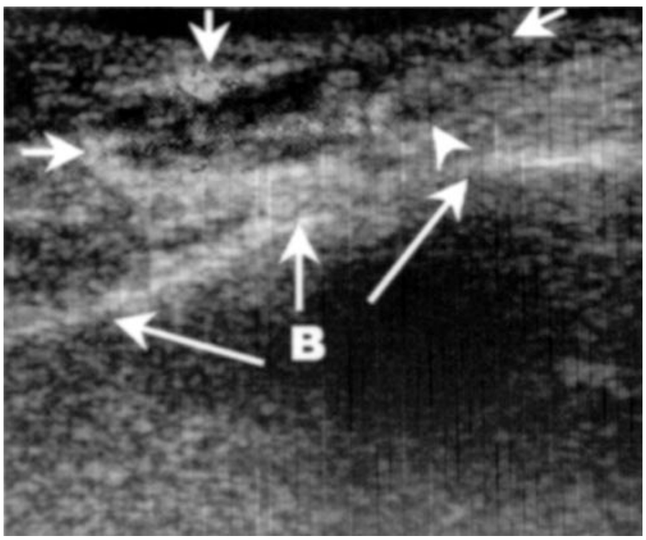


Figure 5. Sarcoid nodule on preauricular area (patient 26). Nodule (short arrows) has an oval heterogeneous appearance similar to a tophus. It is very close to the mandibular bone (B), but there is no bone destruction.

The 4 synovial cysts studied were found in the popliteal area of 4 patients with RA. One presented with fullness in the posterior leg as it had dissected into the calf. The other 3 had palpable popliteal mass sizes that ranged from 1.5 to 2.5 cm. US showed a characteristic boomerang hypoechoic pattern[19] in the transverse view. The cystic swellings originated from the posteromedial aspect of the knee and had a distinct neck situated between the medial head of the gastrocnemius muscle and semimembranosus tendon.

DISCUSSION

Gout is a common disease not usually diagnosed by identification of tophi because tophi are formed in long-standing gouty arthritis with poorly controlled serum uric acid[20,21]. However, in atypical presentations of gouty arthritis with polyarticular disease and nodules, we may want to differentiate them from rheumatoid nodules by needle aspiration. US if confirmed to be characteristic might also play a role in such a diagnosis[17-22].

In our study, the sonographic images of tophi were most often characterized as heterogeneous masses with hypoechoic areas likely due to chalky liquid tophaceous material. Actually, some of these hypoechoic areas could be shown to be due to liquid material as the images changed with aspiration. Occasionally our tophi had calcifications that appeared hyperechoic with acoustic shadowing[23]. Calcification within tophi has been reported, but may not be common[24-26]. The cortical bone erosions noted adjacent to many tophi could represent an important feature of the tophi and could parallel their ability to eventually destroy bone[27].

The reason for a rather hypoechoic appearance of rheumatoid nodules is not clear. These nodules often have hyperechogenic walls. Sanders, *et al* suggested, based on MRI and histologic findings, that this is due to the characteristic central necrosis of rheumatoid nodules[28]. Some subcutaneous rheumatoid nodules were attached closely to the bone surface and in our series were less erosive to bone than were the tophi. Bone erosion has been reported with subcutaneous rheumatoid nodules that occur over bony prominences subjected to repeated mechanical pressure. This is infrequent and usually due to extension of granulomatous invasion[29]. In contrast, tophi have been said to erode more often probably via cytokine liberation. Barthelemy, *et al* reported that 42% of tophi had radiographic changes on bone[30].

US has the potential to be used as a tool to measure the change in size or features after treatment of either gout or RA. Our preliminary sequential studies suggest that findings can be reproducible, and we propose this for further study.

Lipoma images varied in echogenicities in our 2 cases and in the literature[29]; there are many sonographic reports[31–33] that describe features of lipomas as depending on composition of connective tissue and position of the mass. In subcutaneous types, lipomas have an elongated shape and an orientation parallel to the skin with a mostly well demarcated wall that is not as hyperechoic as in a rheumatoid nodule[34]. Although their features were not specific, when combined with a good clinical history and examination they may be strongly supportive for the diagnosis.

This is the first detailed study to describe and compare the ultrasonographic characteristics of gouty tophi and subcutaneous rheumatoid nodules. The US findings of subcutaneous nodules in our study do not show anything absolutely pathognomonic for RA nodules or gouty tophi. However, there are some US characteristics that can be combined with clinical findings to aid in diagnosis. Rheumatologists can use US for a baseline assessment of subcutaneous nodules in patients who decline aspiration or biopsy or prior to other diagnostic techniques. The full potential of sonography for rheumatology needs further study.

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